TCT-121

Heparin Bridging Or Uninterrupted Oral Anticoagulation During Coronary Stenting. The AFCAS Trial

Pekka Porela[1], Axel Schlitt[2], Andrea Rubboli[3], Heli Lahtela[1], Matti Niemelä[4], Pasi Karjalainen[5], Paulus Kirchhof[6], KEJ Airaksinen[1], AFCAS Study Group
[1]Turku University Hospital, Turku, Finland[2]Martin Luther-University, Halle, Germany[3]Ospedale Maggiore, Bologna, Italy[4]Oulu University Hospital, Oulu, Finland[5]Satakunta Central Hospital, Pori, Finland[6]Clinic Münster, Münster, Germany

Purpose: Uninterrupted oral anticoagulation (UAC) is increasingly used during coronary stenting, although bridging therapy (BT) is still a common recommendation.
Methods and Results: In this interim analysis of AFCAS multicenter European prospective Registry we included patients with atrial fibrillation who underwent coronary stenting during UAC (N= 205) or using BT (N=80). In the BT group, warfarin was withdrawn for a mean of 4 (range 1-15) days prior to PCI (mean INR 1.9). In the UAC group, mean procedural INR was 2.2 (p=0,000). The groups were comparable with respect to the baseline characteristics (mean age 73 years), but there were significant procedural differences between the groups. Non-major bleeding and access site complications were more common in the BT group, but there were no other significant differences in the hospital outcome. Femoral access (p=0.01) and age (p=0.04) were the significant independent predictors for in-hospital complications.

In-hospital complications in the study groups.

	BT	UAC	p
Cardiac Death	1 (1,3%)	1 (0,5%)	0,5
MACE	4 (5%)	5 (2%)	0.3
Stroke	0	1 (0,5%)	1
Major Bleeding	1 (1 %)	3 (2%)	1
Non-major Bleeding	11 (14%)	6 (3%)	0.001
Access site compl	21 (27%)	15 (7%)	<0.001

Conclusion: Our study shows that stenting is a safe procedure during UAC with no excess bleeding or thrombotic complications.

TCT-122

Prolonged Bivalirudin Infusions After In-lab Clopidogrel Loading: Safety of Real-world PCI Antithrombotic Practices

Homam Ibrahim[1], Jose G Diez[2,3], Jonathan A Aliota[2], Maithili H Shenoy[1], James M Wilson[2,1], R. David Fish[2,1]
[1]St.Lukes Episcopal Hospital, Houston, TX;[2]Texas Heart Institute, Houston, TX;[3]Baylor College of Medicine, Houston, TX

Background: In PCI patients pretreated with clopidogrel bivalirudin is safe and effective procedural antithrombotic therapy. However, clopidogrel loading is commonly given in the cath lab and bivalirudin stopped at the end of case. We evaluated the use of prolonged (PRG) bivalirudin infusions (120 - 240 minute total infusion times) from the loading dose of clopidogrel as a means of compensating for incomplete thienopyridine effect, as compared to standard (STD) therapy during PCI.
Methods: Prospective data on patients undergoing acute or elective PCI. All patients received ASA 325 mgs and clopidogrel loading dose of 600 mgs, and bivalirudin bolus 0.75 mg/kg followed by infusion of 1.75 mg/kg/h. Patients were divided into two strategies: STD and PRG > 120 min bivalirudin infusions.
Results: A total of 81 consecutive cases were evaluated. Of those, 31 patients had STD mean infusion of 45.3 min, 50 had infusions of ≥120 min (mean 198.1). In the 31 pts who received STD had a mean reduction in hemoglobin of 0.86 gm/dl ± 1.01 gm/dl vs PRG infusion 0.98 gm/dl ± 0.84 gm/dl, (P=0.5892). In the STD there was one TIMI minor bleed, and 4 cases who needed target lesion revascularization (TLR) within 18 months. In the PRG there were no TIMI minor bleeds, and no 18-month TLR. There were no significant differences in cardiac enzyme levels, GUSTO scale bleeds or in-hospital MACE.
Conclusions: Prolonged infusions of bivalirudin (>120 minutes) during PCI did not increase bleeding, post-procedural platelet counts or PCI-related thrombocytopenia. There were fewer total events in the PRG infusion arm, due to decreased TLR. Prolonged bivalirudin infusion times, from clopidogrel loading, provides extended peri-procedural antithrombin therapy. This pilot study suggests that such infusions do not cause an increase in bleeding, and may contribute to an overall lower event rate where patients may be loaded with clopidogrel in-lab. There is a need for larger, randomized trials to validate the efficacy of this strategy.

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TCT-123

Vasomotor Function Following Paclitaxel-coated Balloon Post-dilatation in Porcine Coronary Stent Model

Takamitsu Nakamura[1], Brigitta C Brott[2], Xinhua Yin[1], Jinsheng Li[1], Jack P Chen[1], Jaipal Sigh[1], Spencer B King, III[1], Nicolas Chronos[1], Dongming Hou[1]
[1]Saint Joseph's Translational Research Institute, Atlanta, GA;[2]University of Alabama, Birmingham, AL

Background: Drug-eluting stents (DES) have been associated with impaired endothelial function 6-12 months after stent deployment. It is unclear whether this abnormal vasomotor function is mitigated by reduced duration of exposure to drug release. The purpose of this study was to evaluate endothelial function after post-dilation of bare metal stents with paclitaxel-coated balloons (PCB) or non-drug coated balloons (non-DCB) in a porcine model.
Methods: Thirteen pigs underwent bare-metal stent (BMS) implantation (S/A, 1.1:1; n=30 arteries), followed by post-dilation (B/A, 1.2:1) with either PCB (SeQuent®, n=17) or non-DCB (n=13). Five pigs with unstented, untreated arteries (n=14) were used as controls. Coronary vasomotor function was assessed for all stented arteries one month after implantation, using acetylcholine (Ach) at two doses (10^{-7} and 10^{-6} M) and nitroglycerin (NTG, 200 µg). Measurements were obtained for regions of the vessel, as measured from the distal stent edge: 5-10 mm (D1), and 10-15 mm (D2). Animals were terminated for histopathologic and histomorphometric analysis.
Results: Angiographic late loss (p=0.38) and histologic area stenosis (p=0.22) were not different between PCB and non-DCB. However, the % diameter change in response to Ach was significantly diminished with PCB (p<0.05, respectively) at the D1 and D2 regions, when compared with either the non-DCB or naïve arteries. There were no differences between non-DCB and naïve. Histopathology, inflammatory cell infiltration and intramural fibrin deposition were significantly greater after PCB than non-DCB (p<0.05). In addition, the inflammatory response in the stented segment correlated with the degree of % diameter change in response to Ach, at both the D1 and D2 regions.
Conclusions: Post-dilation of BMS with PCB was associated with an impaired vasodilatory response to Ach distal to the treated segments in this pig model. The vasodilatory response after post-dilation with non-DCB was not different than control, naïve arteries. These findings suggest a potential adverse influence of PCB on downstream coronary endothelial function.

TCT-124

Improved Functional Re-endothelialization Following Stenting With Xience V® In Comparison To Endeavor Resolute In An Atherosclerotic Rabbit Double Injury Model

Christophe Van Dyck[1], Vicky Hoymans[1,2], Geert Frederix[2], Jean-Pierre Timmermans[1], Christiaan Vrints[1,2]
[1]University of Antwerp, Antwerp, Belgium[2]Antwerp University Hospital, Edegem, Belgium

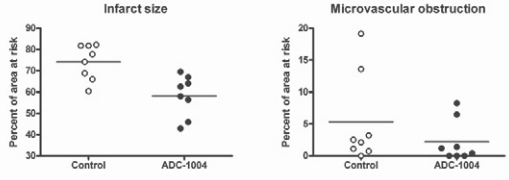
Aims: To evaluate differences in strut coverage and endothelialization to two different second generation polymer based drug-eluting stents (DES) in an atherosclerotic rabbit double injury iliac artery model.
Methods and Results: Twenty- four New Zealand White rabbits were subjected to balloon denudation of the iliac arteries and 1% high cholesterol plus 6% peanut oil feeding. At week five, the cholesterol diet was reduced to 0.025% for the remainder of the in-life-phase. Eight weeks later, single everolimus-eluting stents (EES, XIENCE V®), zotarolimus eluting stents (ZES, Endeavor Resolute®), bare metal stents (BMS, VISION®) were implanted bilaterally and expanded to a nominal stent diameter (3.0×12mm) with a target balloon to artery ratio of 1.3:1. Animals were then euthanized at 28-days post-implant, and the harvested vessels were analyzed by scanning electron microscopy and immunohistochemical staining for von Wildebrand factor (vWF). Additional stainings with hematoxylin eosin (inflammatory cells), Movat Pentachrome (focal fibrin), and Masson's Trichrome (eosinophilic infiltrates) were completed.
In all animals, the lesion underlying the stent was well established with similar Stary type IV lesion grades indicating the presence of a confluent extracellular lipid core. At 28 days, in all stent groups, struts were completely covered by neointima as assessed by SEM. Endothelial coverage assessed by vWf was greater for EES (65% coverage, p = 0.184) and BMS (79% coverage, p= 0.005) vs. ZES (56 % coverage). Notably, the extent of inflammation between stents was greater for ZES indicated by a greater monocyte adherence (p = 0.0005, EES vs. ZES). Adhered monocytes tended to be exposed in areas absent of functional endothelium, suggesting an inverse correlation between rate of endothelialization and inflammation. Finally, EES showed fewer focal fibrin deposition (p = 0.009, EES vs. BMS; p= 0.06, ZES vs. BMS) and absence of intra-intimal haemorrhage.
Conclusions: Histopathologic results of EES and ZES iliac artery implants in an atherosclerotic rabbit model showed significantly less endothelial coverage and greater inflammation in ZES vs. EES.

TCT-125

Inhibition of C5a Related Neutrophil Activation by ADC-1004 Reduces Myocardial Injury in a Porcine Ischemia-Reperfusion Model

Jesper van der Pals[1], Sasha Koul[1], Patrik Andersson[1], Matthias Götberg[1], Joey F A Ubachs[1], Mikael Kanski[1], Håkan Arheden[1], Göran K Olivecrona[1], Bengt Larsson[1,2], David Erlinge[1]
[1]Lund University Hospital (SUS), Lund, Sweden[2]Alligator Bioscience AB, Lund, Sweden

Background: Polymorphonuclear neutrophils, stimulated by the activated complement factor C5a, have been implicated in cardiac ischemia/reperfusion injury. ADC-1004 is a competitive C5a receptor antagonist that has been shown to inhibit complement related neutrophil activation. Acting on the circulating neutrophils, ADC-1004 shields the neutrophils from C5a activation already before they enter the reperfused area. We investigated if treatment with ADC-1004, according to a clinically applicable protocol, would reduce infarct size and microvascular obstruction in a large animal myocardial infarct model.
Methods: In 16 anesthetized pigs (40-50kg), a percutaneous coronary intervention balloon was inflated in the left anterior descending artery for 40 minutes. Twenty minutes after balloon inflation the pigs were randomized to an intravenous bolus administration of ADC-1004 (175 mg, n=8) or saline (9 mg/ml, n=8). Area at risk (AAR) was evaluated by ex-vivo single photon emission computed tomography (SPECT). Infarct size and microvascular obstruction were evaluated by ex-vivo magnetic resonance imaging (MRI). The observers were blinded to the treatment at randomization and analysis.
Results: ADC-1004 treatment reduced infarct size by 21% (58.3±3.4 vs 74.1±2.9 %AAR, p=0.007). Microvascular obstruction was insignificantly reduced by 58% in the ADC-1004 group (2.2±1.2 vs 5.3±2.5 %AAR, p=0.23). The plasma concentration of ADC-1004 was 83±8 nM at sacrifice (target approximately 90 nM). Heart rate, mean arterial pressure, cardiac output and blood-gas data were similar between the groups.



Conclusion: ADC-1004 treatment, according to a clinically applicable protocol, reduces myocardial ischemia-reperfusion injury. ADC-1004 thus represents a novel treatment strategy of myocardial infarct with potential clinical applicability.